

REMARKS

Claims 7-10, 18-23, 25-27, 30-33, 36, and 37 are pending.

The specification has been amended to update the status of the parent application, which is now abandoned.

The language in Claim 7 is supported on page 15, lines 1 and 9-15. The language in claim 18 is supported on page 15, lines 1 and 9-15 and page 29, lines 22-23. The language in claim 25 is supported on page 9, lines 18-20. Claim 33 is supported page 7, lines 33-page 8, line 2, page 9, lines 10-12. Claim 36 is supported in the specification on the pages listed above and further on page 33, line 17-18. Claim 37 is supported on page 40, lines 18-21.

No new matter is provided by this amendment.

I. PRIORITY

The examiner states that Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 USC 120 as follows.

- A. *The examiner states that the application fails to include the status of US Patent Application No. 09/242,977.*

At the time this application was filed, that application was not abandoned and thus, the status information was correct at the time of filing.

The specification is being amended herewith to indicate the status of application number 09/242,977.

Applicants request reconsideration and withdrawal of this rejection.

- B. *The examiner argues that US Patent Application No. 08/708,188 filed on September 6, 1996 does not provide adequate support under 35 USC 112 for claims 25 and 26 of this application because it does not recite the term "helper-free" and thus does not provide written support for these claims.*

The examiner argues claims 25 and 26 only have priority to PCT/US97/15692.

Applicants request reconsideration and withdrawal of this rejection.

Although the phrase “helper-free” is not found, *ipsis verbis*, in the referenced application, there is written support for this language. For example, this application recites:

“the inventors have demonstrated that intramuscular injection of purified rAAV (i.e., rAAV which is substantially free of contamination with adenovirus or wild-type AAV) leads to efficient transduction of postmitotic muscle fibers with the provirus integrating into chromosomal DNA leading to very prolonged transgene expression. According to the invention, this is accomplished without significant inflammation or activation of immunity to the transgene product, despite the fact that the product may be a neoantigen, which in the context of adenovirus is extremely immunogenic.” [page 7, lines 13-24 of US Patent Appln No. 08/708,188].

The presence of the precise words in the claim is not a requirement for written description where the meaning of the words is clear from the specification.

Reconsideration and withdrawal of this rejection is requested.

II. CLAIM OBJECTIONS

Claim 27 has been amended to correct the phrase for a dependent claim.

Applicant respectfully traverse the objection to the recitation of “less than” in this claim for the reasons discussed below.

Withdrawal of this objection is requested.

III. CLAIM REJECTIONS – 35 USC 112

- A. Claims 27 and 32-35 are rejected under 35 USC 112, first paragraph, as failing to comply with the written description requirement.

1. *The examiner argues that the limitation "less than 1 infectious unit of wild-type AAV per 10⁹ rAAV" in new claim 27 is not supported by the as-filed specification. The examiner argues that the support relied upon by applications is limited to a rAAV-F.IX.*

Applicants disagree with the Examiner's contention based on the recent decision in *Capon v. Eshhar*, No. 03-1480, -1481, 2005 U.S. App. LEXIS 16865 (Fed. Cir. Aug. 12, 2005), pertinent to the issue of written description under 35 U.S.C. 112, first paragraph." In *Capon*, the Federal Circuit vacated a decision of the Board of Patent Appeals and Interferences (Interference No. 103,887) that held the claims of both parties to the interference invalid for lack of written description. The claims at issue were directed to chimeric DNA designed to enhance the immune response by providing cells with specific cell-surface antibodies in a form that could penetrate diseased sites (e.g., solid tumors). During the interference proceeding, the parties explained that their chimeric genes were produced by selecting and combining known heavy- and light-chain immune-related DNA segments using known procedures, and provided expert testimony explaining that the principle of forming chimeric genes from selected segments of DNA was known, as well as the methods of identifying, selecting, and combining the desired segments of DNA. However, the Board held that both party's claims were broader than the specific examples because neither party's specification provided the requisite description of the full scope of the chimeric DNA or encoded proteins by reference to knowledge in the art of the structure, formula, chemical name, or physical properties of the DNA or the proteins.

In *Capon*, the appeal of the Board's decision to the Federal Circuit, the Board's decision was vacated. The Federal Circuit stated that "the law must take cognizance of the scientific facts" (*Capon*, p. 7), that "the 'written description' require[s] the patentee [to] describe the invention; it does not state that every invention must be described in the same way" (*Capon*, p. 8), and that "[i]t is not necessary that every permutation within a generally operable invention be effective in order for an inventor to

obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention" (Capon, p. 9). Applicants additionally request reconsideration of the outstanding rejection in view of the rationale provided in Capon.

Reconsideration and withdrawal of this rejection is requested.

2. *The examiner argues that new claims 32-35 embrace a genus of administration routes, genus of muscle cells, and a genus of transgenes, but that the specification only recites "absence of inflammation upon administration of therapeutic doses of vector" in relation to a vector containing lacZ following intramuscular injection.*

Applicants respectfully traverse this rejection.

The claims now recite intramuscular introduction into skeletal muscle cells.

Page 29, lines 10-23 refers to adenoviruses eliciting a cascade of immunological responses leading to destructive cellular and humoral immunity. While the following example illustrates this with a vector carrying lacZ, this does not obviate the more general nature of the first paragraph of Example 5.

Reconsideration and withdrawal of this rejection is requested.

3. *Claims 7-10 and 12-24 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification. The examiner argues that "at least as free of adenoviral helper virus as is obtained . . ." is broader than performing four rounds of cesium chloride gradient centrifugation, that "at least" has no upper limit and that the limitation encompasses other methods not disclosed in the specification. The declarations are deemed inadequate because they do not address the new matter rejection.*

Applicants respectfully traverse this rejection.

The claims recite that the claims recite "as free of adenovirus helper virus . . ."

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Reconsideration and withdrawal of this rejection is requested.

4. *Claims 32-35 are rejected as lacking enablement for a method of expressing a transgene in all muscle cells.*

Applicants respectfully traverse this rejection.

The examiner argues that the invention is enabling for a method of expressing a transgene in a skeletal muscle cell of a mammal using intramuscular administration of an rAAV, wherein the rAAV is purified of adenoviral helper such that an immune response is absent.

In view of the present amendment and remarks provided above, Applicants request reconsideration and withdrawal of this rejection in view.

IV. CLAIM REJECTIONS – 35 USC §103

- A. *Claims 25 and 26 are rejected under 35 USC §103(a) as being unpatentable over Chiorini, (AAB) taken with Dwarki, US Patent 6,221,646.*

Applicants respectfully traverse this rejection.

As amended, the claims clarify that the method of the invention utilizes rAAV prepared using a helper virus and purified therefrom.

For the reasons set forth above, Applicants believe that these claims are entitled to the earliest priority date and thus, Dwarki is not available as prior art.

Nevertheless, the combined teachings of Chiorini and Dwarki fail to teach or suggest use of such a composition, or the purification of rAAV such that an immune response to helper virus is absent upon administration of the helper-free rAAV.

Reconsideration and withdrawal of this rejection is requested.

- B. *Claims 7-10, 18-23 and 25-35 are rejected under 35 USC §103(a) as being unpatentable over Podsakoff et al (AI) taken with Colosi, US Patent 6,004,797.*

Applicants respectfully traverse this rejection.

The combined teachings of Podsakoff and Colosi fail to teach or suggest use of such a rAAV prepared using a helper virus and purified therefrom, in the absence of a cytotoxic immune response to helper virus, immune response to the helper virus is absent, in the absence of a destructive immune response to the rAAV-transduced cell, and in the absence of inflammation caused by contaminating helper adenovirus.

Reconsideration and withdrawal of this rejection is requested.

- C. *Claims 7-10, 12-17 and 24-26 are rejected under 35 USC §103(a) as being unpatentable over Podsakoff et al (AI) taken with Colosi, as applied to claims 7-10, 18-23 and 23-25 and further in view of Fang et al 1995 (CS) and Kay et al, US Patent 5,980,886.*

Applicants respectfully traverse this rejection.

The combination of Fang and Kay to the previously discussed combination of Podsakoff and Colosi fails to suggest the use of such a rAAV prepared using a helper virus and purified therefrom, in the absence of a cytotoxic immune response to helper virus, immune response to the helper virus is absent, in the absence of a destructive immune response to the rAAV-transduced cell, and in the absence of inflammation caused by contaminating helper adenovirus.

Reconsideration and withdrawal of this rejection is requested.

V. DOUBLE PATENTING

Claims 7-10 and 12-24 and claims 25-35 are rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-4 of US Patent 5,866,552.

The examiner has acknowledged applicants' request that this rejection be deferred until allowance is acknowledged.

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The Director of the US Patent and Trademark Office is hereby authorized to charge any fee due to Deposit Account 08-3040.

Respectfully submitted,

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